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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,893	01/17/2001	Shih-Chieh Hung	11709-003001	6011

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Examiner-Initiated Interview Summary	Application No.	Applicant(s)	
	09/761,893	HUNG ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Jennifer Dunston*.

(2) *Ardin Marschel*.

(3) *Jean Witz*.

(4) _____.

Date of Interview: *19 March 2012*.

Type: ☒ Telephonic ☐ Video Conference
☐ Personal [copy given to: ☐ applicant ☐ applicant's representative]

Exhibit shown or demonstration conducted: ☐ Yes ☒ No.
If Yes, brief description: _____.

Issues Discussed ☐101 ☐112 ☐102 ☒103 ☐Others
(For each of the checked box(es) above, please describe below the issue and detailed description of the discussion)

Claim(s) discussed: *1,4,6,9-11,34,35 and 38*.

Identification of prior art discussed: *Prockop et al. (US Patent No. 7,374,973), and Pittenger et al. Science, Vol. 284, pages 143-147, April 1999*.

Substance of Interview
(For each issue discussed, provide a detailed description and indicate if agreement was reached. Some topics may include: identification or clarification of a reference or a portion thereof, claim interpretation, proposed amendments, arguments of any applied references etc...)

See Continuation Sheet.

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

☐ Attachment

/Jennifer Dunston/ Primary Examiner Art Unit 1636	

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: The pre-appeal brief asserts that the specification teaches "isolated MSCs can proliferate without differentiation and reach confluence even after 12 passages."

The present claims do not require culture to confluence for 12 passages.

The specification states, "The cells maintain a normal proliferation and undifferentiation status during culture expansion even at passage 12." See page 14, lines 23-25.

Prockop et al (US Patent No. 7,374,937) teaches the propagation of human bone marrow MSCs with re-plating at a density of 5 x 10^3 cells/cm^2 with growth to near confluence (e.g., column 22, lines 19-33). This is referred to as High Density Plating (e.g., paragraph bridging columns 21-22). Some MSC samples only proliferated for four population doublings, and other proliferated over 15 cell doublings from frozen cell stocks (e.g., paragraph bridging columns 23-24; Fig. 1). Differentiation assays were carried out with "late passage MSCs (e.g., passage 12)." The "late passage MSCs" retained the ability to differentiate to osteoblasts; however, the MSCs failed to differentiate into adipocytes (e.g., column 24, lines 57-67).

In Example 2, Prockop et al state the following:
The data disclosed in this example demonstrate that plating MSCs at a low density (e.g., between about 0.5 to about 10 cells per square centimeter) increases, relative to prior art culture techniques, the number of population doublings which the MSCs can undergo without also undergoing differentiation. As a result, differentiatable MSCs can be expanded in culture to a far greater extent than they can using prior art culture/expansion methods. (Column 27, lines 29-37).

Prockop et al state the following at column 29, lines 27-24:
Moreover, the number of cell doublings is increased three-fold relative to prior art culture conditions, as indicated in FIG. 9. Therefore, the MSC culture/expansion method described in this example, allows greater number of MSCs to be generated, and including a greater percentage of differentiatable (i.e., multipotential) cells than do prior art culture methods.

Using the "low density" method, Prockop et al teach the following at column 16, lines 49-61:
There is no theoretical limit to the number of rounds of expansion and harvest that can be performed. However, it is recognized that because each expansion/harvest cycle will significantly increase the number of MSCs available (i.e., by 10-fold, 100-fold, or more), a geometrically increasing amount of growth medium and growth surface will be required during sequential expansion/harvest cycles if all expanded MSCs are to be further expanded. Thus, it is recognized that for most applications, no more than about 10 cycles of expansion and harvest will normally be necessary, and as few as 1, 2, 3 or 4 cycles will be sufficient for many applications (e.g., cell therapy or gene therapy).

Prockop et al teach a method that allows a greater number of MSCs to be generated, including a greater percentage of differentiatable (i.e., multipotential cells) than prior art culture methods, one would have expected the culture conditions taught by Prockop et al to provide culture to confluence for 12 passages without differentiation.

Prockop et al teach a lower density is required to obtain more cells. However, the prior art teaches that cells plated at the higher density (about 10^3 cells/cm^2) for 12 passages lose the ability to differentiate to adipocytes (Prockop et al. column 24, lines 57-67). The present specification does not provide evidence that the cells re-plated at 4 x 10^3-10^4 cells/cm^2 for 12 passages are able to differentiate to adipose or cartilage as presently claimed in claim 9. The specification teaches differentiation of the MSCs 14 days following the first passage (Example 4). Other art of record teaches reduced ability to differentiate after about 19 to 21 population doublings when cells are plated at 1.5 million to 6 million cells per 150-mm dish (Pittenger et al. Science, Vol. 284, pages 143-147, April 1999; e.g., page 145, left column).